
Sequence Listing could not be accepted due to errors.

See attached Validation Report.

If you need help call the Patent Electronic Business Center at (866)

217-9197 (toll free).

Reviewer: Keisha Douglas

Timestamp: [year=2008; month=8; day=11; hr=19; min=34; sec=16; ms=85;]

Reviewer Comments:

210> 231

<211> 22

<212> DNA

<213> Artificial Sequence

<220>

<221> misc_feature

<222> 1; 22

<223> EMCV Probe: n at position 1 is a 5-carboxyfluorescein(FAM)-modified deoxycytidylate; n at position 22 is an N,N,N',N'-tetramethyl-6-carboxyrhodamine(TAMRA)-modified deoxythymidylate.

<400> 231

nagccgtca agacccaacc gcn

22

Validated By CRFValidator v 1.0.3

Application No: 10658834 Version No: 4.0

Input Set:

Output Set:

Started: 2008-07-01 15:59:41.713 **Finished:** 2008-07-01 16:00:20.896

Elapsed: 0 hr(s) 0 min(s) 39 sec(s) 183 ms

Total Warnings: 199

Total Errors: 3

No. of SeqIDs Defined: 1306
Actual SeqID Count: 1306

Error code		Error Description									
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W	213	Artificial	or	Unknown	found	in	<213>	in	SEQ	ID	(4)
W	213	Artificial	or	Unknown	found	in	<213>	in	SEQ	ID	(5)
W	213	Artificial	or	Unknown	found	in	<213>	in	SEQ	ID	(6)
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W	213	Artificial	or	Unknown	found	in	<213>	in	SEQ	ID	(11)
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W	213	Artificial	or	Unknown	found	in	<213>	in	SEQ	ID	(15)
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W	213	Artificial	or	Unknown	found	in	<213>	in	SEQ	ID	(18)
W	213	Artificial	or	Unknown	found	in	<213>	in	SEQ	ID	(19)
W	213	Artificial	or	Unknown	found	in	<213>	in	SEQ	ID	(20)
W	213	Artificial	or	Unknown	found	in	<213>	in	SEQ	ID	(21)

Input Set:

Output Set:

Started: 2008-07-01 15:59:41.713

Finished: 2008-07-01 16:00:20.896

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Error code Error Description This error has occured more than 20 times, will not be displayed W 401 Unrecognized range formatin <222> in SEQID (231) E 224 <220>, <223> section required as <213> has Artificial sequence or Unknown in SEQID (231) E 342 'n' position not defined found at POS: 1 SEQID(231) E 342 'n' position not defined found at POS: 22 SEQID(231)

SEQUENCE LISTING

<110> Gantier, Rene Guyon, Thierry Drittanti, Lila Vega, Manuel <120> Rational Evolution of Cytokines for Higher Stability, the Cytokines Encoding Nucleic Acid Molecules <130> 119365-00005/922 <140> 10658834 <141> 2003-09-08 <150> 60/457,135 <151> 2003-03-21 <150> 60/409,898 <151> 2002-09-09 <160> 1306 <170> FastSEQ for Windows Version 4.0 <210> 1 <211> 165 <212> PRT <213> Homo sapiens <400> 1 Cys Asp Leu Pro Gln Thr His Ser Leu Gly Ser Arg Arg Thr Leu Met 5 10 Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp 25 Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln 40 Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu 65 70 75 Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu 85 90 Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys 105 Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu 120 Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg 135 Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser 155

<210> 2

<211> 165

Leu Arg Ser Lys Glu

165

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<212> PRT
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Cys Ala Leu Pro Gln Thr His Ser Leu Gly Ser Arg Arg Thr Leu Met
                                 10
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
          20
                              25
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
                          40
Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe
                      55
Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu
                  70
                                     75
Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu
             85
                                 90
Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys
                             105
Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu
                          120
                                  125
       115
Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg
                      135
                                      140
Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser
                                     155
                 150
Leu Arg Ser Lys Glu
              165
<210> 3
<211> 165
<212> PRT
<213> Artificial Sequence
<220>
<223> P4A Mutant IFN-alpha 2b
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Cys Asp Leu Ala Gln Thr His Ser Leu Gly Ser Arg Arg Thr Leu Met
                5
                                 10
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
                              25
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
                         40
Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe
                      55
Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu
                  70
                                      75
Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu
              8.5
                                  90
Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys
                              105
Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu
                         120
Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg
   130 135 140
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Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser

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155
145
                   150
                                                           160
Leu Arg Ser Lys Glu
              165
<210> 4
<211> 165
<212> PRT
<213> Artificial Sequence
<223> Q5A Mutant IFN-alpha 2b
<400> 4
Cys Asp Leu Pro Ala Thr His Ser Leu Gly Ser Arg Arg Thr Leu Met
                                  10
Leu Leu Ala Gln Met Arq Arq Ile Ser Leu Phe Ser Cys Leu Lys Asp
           2.0
                               25
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
                           4.0
Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe
                       55
Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu
                   70
                                       75
Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu
              85
                                  90
Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys
          100
                              105
Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu
                120
                                    125
       115
Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg
                       135
                                          140
Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser
                                      155
                   150
Leu Arg Ser Lys Glu
              165
<210> 5
<211> 165
<212> PRT
<213> Artificial Sequence
<220>
<223> T6A Mutant IFN-alpha 2b
<400> 5
Cys Asp Leu Pro Gln Ala His Ser Leu Gly Ser Arg Arg Thr Leu Met
                5
                                  10
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
                          40
Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe
                       55
Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu
                  70
                                       75
Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu
                                  90
Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys
```

105

100

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Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu
                       120
Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg
           135
                              140
Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser
145 150
                          155
Leu Arg Ser Lys Glu
             165
<210> 6
<211> 165
<212> PRT
<213> Artificial Sequence
<223> H7A Mutant IFN-alpha 2b
<400> 6
Cys Asp Leu Pro Gln Thr Ala Ser Leu Gly Ser Arg Arg Thr Leu Met
                               10
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
                           25
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
                        40
Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe
                    55
Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu
                 70
                                   75
Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu
          85
                   90
Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys
                           105
Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu
                               125
      115
                      120
Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg
                    135
                               140
Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser
    150
                                  155
Leu Arg Ser Lys Glu
             165
<210> 7
<211> 165
<212> PRT
<213> Artificial Sequence
<220>
<223> S8A Mutant IFN-alpha 2b
<400> 7
Cys Asp Leu Pro Gln Thr His Ala Leu Gly Ser Arg Arg Thr Leu Met
              5
                               10
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
                            25
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
                       40
Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe
   50 55 60
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Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu

```
65
                  70
Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu
           85
                                90
Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys
               105
Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu
                        120
Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg
                              140
                    135
Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser
145 150
                                   155
Leu Arg Ser Lys Glu
             165
<210> 8
<211> 165
<212> PRT
<213> Artificial Sequence
<220>
<223> L9A Mutant IFN-alpha 2b
<400> 8
Cys Asp Leu Pro Gln Thr His Ser Ala Gly Ser Arg Arg Thr Leu Met
              5
                                10
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
                             25
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
                40
Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe
                     55
Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu
                                    75
                 70
Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu
        85
                                90
Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys
                             105
Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu
              120
Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg
          135
Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser
145
                  150
                                    155
Leu Arg Ser Lys Glu
             165
<210> 9
<211> 165
<212> PRT
<213> Artificial Sequence
<223> G10A Mutant IFN-alpha 2b
<400> 9
Cys Asp Leu Pro Gln Thr His Ser Leu Ala Ser Arg Arg Thr Leu Met
               5
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Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
                           25
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
               40
Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe
                    55
Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu
                      75
                 70
Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu
                               90
Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys
                          105
         100
Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu
              120
Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arq
          135
Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser
         150
145
                                 155
Leu Arg Ser Lys Glu
             165
<210> 10
<211> 165
<212> PRT
<213> Artificial Sequence
<220>
<223> S11A Mutant IFN-alpha 2b
<400> 10
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Ala Arg Arg Thr Leu Met
             5
1
                               10
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
                           25
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe
                    55
Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu
65 70
                                  75
Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu
                               90
Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys
       100 105 110
Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu
Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg
                            140
          135
Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser
145 150
                                  155
Leu Arg Ser Lys Glu
<210> 11
<211> 165
<212> PRT
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<213> Artificial Sequence

<223> R12A Mutant IFN-alpha 2b

<400> 11

Cys Asp Leu Pro Gln Thr His Ser Leu Gly Ser Ala Arg Thr Leu Met

1 5 10 15

Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30

Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
35 40 45

Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe 50 55 60

Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu 65 70 75 80

Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu 85 90 95

Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys
100 105 110

Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu 115 120 125

Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg 130 135 140

Leu Arg Ser Lys Glu

165

<210> 12

<211> 165

<212> PRT

<213> Artificial Sequence

<220>

<223> R13A Mutant IFN-alpha 2b

<400> 12

Cys Asp Leu Pro Gln Thr His Ser Leu Gly Ser Arg Ala Thr Leu Met

1 5 10 15

Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp 20 25 30

Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
35 40 45

Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe 50 60

Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu 65 70 75 80

Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu

85 90 95

Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys 100 105 110

Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu 115 120 125

Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg 130 135 140

Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gl